

The Johns Hopkins Hospital,

Baltimore, April 13/97.

Dear Dr. Osler,

The following is, in brief, a description of the leprosy nodules in the skin and subcutaneous tissue of the patient at present in Ward I. You already know that cover-slip preparations made by smearing the excised tissue from the arm on cover-slips and stained by Gram's and Ziehl-Neelsen's methods showed many bacilli having the character of the *B. leprae*.

The sections of the skin and subcutaneous tissue containing the tubercles were stained in haematoxylin and eosine and in carbol-fuchsin and methylene blue. As regards the first: - The tubercles are situated chiefly in the subcutaneous areas and adipose tissues; they are usually discrete and always well-preserved.

Evidences of disease were not met with.
The tubercles are made up of cells of the
epithelioid type, usually with single nuclei,
but a rather unusual number of multi-
nucleated cells are found in certain tubercles.
The great majority of these cells - whether single
or multinucleated - show the degeneration
described by Virchow. After the cell proto-
plasm is enormously swollen and crowded
with vacuoles. Then a smaller cell
will have suffered partial cellular degeneration
of its protoplasm. The nodules are sharply cir-
cumcised by the connective tissue in which
they lie altho' in the younger and forming
nodules elongated autogenous appear to be
going on. These are however separated by
more or less tissue from the original and
older tubercles. Blood-vessels are numerous
in the tubercles.

The behavior of certain of the skin structures
is interesting. Sections of sudoriferous glands
are included in the tubercles and there are

at one time quite normal in appearance and at another rapidly filling up with cells resembling the leprosy cells until finally the contours are lost and they become a part of the tubercle. Some of the giant (multinucleated) cells of the tubercles are derived by confluence from the epithelial lining of these glands. They may also be seen to undergo the typical degeneration. The arrectores pilorum are hypothesized, a fact already pointed out by Birchall. Sebaceous glands were very scanty in the sections studied so that nothing especial was made out of their relation to the tubercle formation.

The relation of the bacteria to the lesions are as follows:- In the tubercles ^{present} they are in the usual great numbers. There seems to me to be no reasonable doubt that they exist in the epithelial and giant cells, surrounding the nuclei of these cells. Whether they also affect at times within the nuclei themselves could not be determined. This case agrees with those studied by a host of others (Vernier, Comil, Urua, etc.) inasmuch as the organisms are found not to invade the epithelial cells of the sudoriferous glands and epidermis. However in a tubercle appearance are obtained suggesting a few bacilli in sweat glands; but it is not excluded that the organisms are not in the interstitial tissue between the sections of the cords. On the other hand, the outer sheath (Haarkalg) ^{of the hair} often contains bacilli in considerable numbers. There can be no doubt that Urua is correct in his statement that the bacilli exist in lymph spaces independently of cells. But this condition is found not within the tubercles but in the connective tissue. Small masses of bacteria may be easily dislodged in the tissue spaces. They grow fewer in number and the size of the masses diminish as the epidermis is approached. The bacilli may however be followed to the epithelium of therete layer just below this bacilli are found in tubercles which much resemble in outline, altho' the pigment was wanting, Chromatophores. I think this fact important when it is considered that the bacilli ~~may~~ ^{are} found in ^{this case} fair numbers in the horny layer of the surface of the epidermis. There are two ways in which they may gain entrance through the unbroken skin to the surface. One is demonstrable in this case, namely from the sheath of the hair. The other is by the action of Chromatophores, which it is well known emigrate between the epithelial cells.

and are capable of reaching the surface. On the skin surface the number of bacilli is greatest in the pits where the horny scales are thicker.

The bacilli are found in the smaller blood-vessels in the tubercles. They infiltrate all the coats but exist in greater numbers in the endothelial cells of the veins which often are crowded with them. These vessels are porous.

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I have not seen in my reading a reference to the occurrence of the bacilli on the surface of the intact skin. I should like to study further the epidermal scales from various parts of the body in order to follow their distribution or, if you permit, I shall be glad to assist in the house officer in charge of the care in this study. In any event I shall study more carefully the behavior of the chromatophores or what I take to be these

structures. Perhaps it may be possible to
have them thro' the epidemics.

Sincerely,

Simon Flexner.

P.S. Can you have a set - of Lecture
for you.

S.F.